We claim:

1. A glucose biosensor for in vivo or in vitro use comprising:

a) at least one mutated binding protein and at least one reporter group attached thereto such that said reporter group provides detectable and reversible signal when said mutated binding protein is exposed to varying glucose concentrations; and

b) an analyte permeable matrix entrapping or encapsulating said at least one mutated binding protein.

2. The biosensor of claim 1 wherein said detectable and reversible signal is related to said varying analyte concentrations.

3. The biosensor of claim 1 wherein said mutated binding protein is glucose/galactose binding protein.

4. The biosensor of claim 3 wherein said glucose/galactose binding protein has at least one amino acid substitution.

5. The biosensor of claim 4 wherein said at least one amino acid substitution is selected from the group consisting of a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position 107, a cysteine at position 110, a cysteine at position 112, a cysteine at position 113, a cysteine at position 137, a cysteine at position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, a cysteine at position 292, a cysteine at position 112 and a serine at

position 238, a cysteine at position 149 and a serine at position 238, a cysteine at position 152 and a cysteine at position 182, a cysteine at position 152 and a serine at position 213, a cysteine at position 213 and a cysteine at position 238, a cysteine at position 149 and an arginine at position 213, a cysteine at position 149 and a serine at position 213 and a serine at position 238, and a cysteine at position 149 and an arginine at position 213 and a serine at position 238.

6. The biosensor of claim 5 wherein said binding protein has at least one histidine tag.

7. The biosensor of claim 1 wherein said reporter group is a luminescent label.

8. The biosensor of claim 7 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.

9. The biosensor of claim 7 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

10. The biosensor of claim 7 wherein said luminescent label is covalently coupled to said at least one binding protein and further comprising wherein said at least one binding protein is glucose/galactose binding protein.

11. The biosensor of claim 10 wherein said luminescent label is covalently coupled to said at least one glucose/galactose binding protein by reaction with a member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMRIA (tetramethylrhodamine-5-

iodoacetamide), Quantum Red ™, Texas Red ™, Cy3, N-((2-iodoacetoxy)ethyl)-N-methyl)amino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan), pyrene, Lucifer Yellow, Cy5, Dapoxyl® (2-bromoacetamidoethyl)sulfonamide, (*N*-(4,4-difluoro-1,3,5,7-tetramethyl- 4-bora-3a,4a-diaza-*s*-indacene- 2-yl)iodoacetamide (Bodipy507/545 IA), *N*-(4,4-difluoro-5,7-diphenyl- 4-bora-3a,4a-diaza-*s*-indacene- 3-propionyl)-*N'*-iodoacetylethylenediamine (BODIPY® 530/550 IA), 5-((((2-iodoacetyl)amino)ethyl) amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).

12. The biosensor of claim 2 wherein said analyte is glucose or galactose.

13. The biosensor of claim 1 wherein said analyte permeable matrix is selected from the group consisting of covalently crosslinked hydrogels, dialysis membranes, sol-gels, and combinations thereof.

14. The biosensor of claim 13 wherein said dialysis membranes have a molecular weight cut-off of about 1000 to about 25,000 Daltons.

15. The biosensor of claim 13 wherein said covalently crosslinked hydrogel is selected from the group consisting of polypeptides, polysaccharides, polysaccharide derivatives, polyvinyl alcohol, polyacrylic acid, polyacrylamide, polyethylene glycols, copolymers of styrene and maleic anhydride, copolymers of olefin and maleic anhydride, and copolymers of vinyl ether and maleic anhydride.

16. The biosensor of claim 15 wherein said said polyvinyl alcohol includes poly(vinyl alcohol), N-methyl-4(4'-formylstyryl)pyridinium acetal salts.

17. The biosensor of claim 13 wherein said sol-gel is selected from at least partially cured hydrolytically condensable siloxanes condensed with at least one water soluble organic polyol component.

18. The biosensor of claim 17 wherein said at least one water soluble organic polyol component is selected from glycerol, ethylene glycol, propylene glycol, and polyethylene glycol.

19. The biosensor of claim 17 further comprising at least one water soluble polymer component.

20. The biosensor of claim 19 wherein said at least one water soluble polymer component is selected from polyvinyl alcohol, copolymers of styrene and maleic anhydride, copolymers of olefin and maleic anhydride, and copolymers of vinyl ether and maleic anhydride, poly-(vinylsulfonic acid) salt, and polyvinyl pyrollidone.

21. The biosensor of claim 17 further comprising functionalized silicone additives.

22. The biosensor of claim 21 wherein said functionalized silicone additives contains organic functionality selected from the group consisting of alkyl, aryl, amine, amide, thiol, cyano, carboxyl, ester, olefinic, epoxy, silyl, nitro, and halogen.

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23. A method for glucose detection comprising:

a) providing at least one mutated glucose/galactose binding protein and at least one reporter group attached thereto;

c) entrapping or encapsulating said at least one mutated glucose/galactose binding protein in an analyte permeable matrix;

d) exposing said mutated glucose/galactose binding protein to varying glucose concentrations; and

e) detecting signal from said reporter group

24. The method of claim 23 wherein said detecting comprises reversible signal detection corresponding to said varying glucose concentrations.

25. The method of claim 23 wherein said detecting is continuous, programmed, episodic, or combinations thereof.

26. The method of claim 23 wherein said reversible signal detection to varying glucose concentrations is *in vivo*.

27. The method of claim 23 wherein said glucose/galactose binding protein has at least one amino acid substitution.

28. The method of claim 27 wherein said at least one amino acid substitution is selected from the group consisting of a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position 107, a cysteine at position 110, a cysteine at position 112, a cysteine at position 113, a cysteine at position 137, a cysteine at position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, a cysteine at position 292, a cysteine at position 112 and a serine at position 238, a cysteine at position 149 and a serine at position 238, a cysteine at position 152 and a cysteine at position 182, a cysteine at position 152 and a serine at position 213, a cysteine at position 213 and a cysteine at position 238, a cysteine at position 149 and an arginine at position 213, a cysteine at position 149 and a serine at position 213 and a serine at position 238, and a cysteine at position 149 and an arginine at position 213 and a serine at position 238.

29. The method of claim 28 wherein said glucose/galactose binding protein has at least one histidine tag.

30. The method of claim 23 wherein said at least one reporter group is a luminescent label.

31. The method of claim 30 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.

32. The method of claim 30 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

33. The method of claim 30 wherein said luminescent label is covalently coupled to said at least one glucose/galactose binding protein by reaction with said at least one mutated binding protein and a member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMRIA (tetramethylrhodamine-5-iodoacetamide), Quantum Red ™, Texas Red ™, Cy3, N-((2-iodoacetoxy)ethyl)-N-methyl)amino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan), pyrene, Lucifer Yellow, Cy5, Dapoxyl® (2-bromoacetamidoethyl)sulfonamide, (*N*-(4,4-difluoro-1,3,5,7-tetramethyl- 4-bora-3a,4a-diaza-*s*-indacene- 2-yl)iodoacetamide (Bodipy507/545 IA), *N*-(4,4-difluoro-5,7-diphenyl- 4-bora-3a,4a-diaza-*s*-indacene- 3-propionyl)-*N'*-iodoacetylethylenediamine (BODIPY® 530/550 IA), 5-((((2-iodoacetyl)amino)ethyl) amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).

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34. A composition comprising a mitixure of:

a) a mutated glucose/galactose binding protein having at least one amino acid substitution selected from the group consisting of a cysteine at position 11, a cysteine at position 14, a cysteine at position 19, a cysteine at position 43, a cysteine at position 74, a cysteine at position 107, a cysteine at position 110, a cysteine at position 112, a cysteine at position 113, a cysteine at position 137, a cysteine at position 149, a cysteine at position 213, a cysteine at position 216, a cysteine at position 238, a cysteine at position 287, and a cysteine at position 292; and

b) an analyte permeable matrix.

35. The composition of claim 34 wherein said mutated glucose/galactose binding protein has at least one histidine tag.

36. The composition of claim 34 wherein said mutated glucose/galactose binding protein further has at least one reporter group.

37. The composition of claim 36 wherein at least one reporter group is a luminescent label.

38. The composition of claim 37 wherein said luminescent label has an excitation wavelength of more than about 600 nanometers.

39. The composition of claim 37 wherein said luminescent label has an emission wavelength of more than about 600 nanometers.

40. The composition of claim 37 wherein said luminescent label is covalently coupled to said at least one glucose/galactose binding protein by reaction with said at least one mutated binding protein and a member selected from the group consisting of fluorescein, coumarins, rhodamines, 5-TMRIA (tetramethylrhodamine-5-iodoacetamide), Quantum Red ™, Texas Red ™, Cy3, N-((2-iodoacetoxy)ethyl)-N-methyl)amino-7-nitrobenzoxadiazole (IANBD), 6-acryloyl-2-dimethylaminonaphthalene (acrylodan), pyrene, Lucifer Yellow, Cy5, Dapoxyl® (2-bromoacetamidoethyl)sulfonamide, (*N*-(4,4-difluoro-1,3,5,7-tetramethyl- 4-bora-3a,4a-diaza-*s*-indacene- 2-yl)iodoacetamide (Bodipy507/545 IA), *N*-(4,4-difluoro-5,7-diphenyl- 4-bora-3a,4a-diaza-*s*-indacene- 3-propionyl)-*N'*-iodoacetylethylenediamine (BODIPY® 530/550 IA), 5-((((2-

iodoacetyl)amino)ethyl) amino)naphthalene-1-sulfonic acid (1,5-IAEDANS), and carboxy-X-rhodamine, 5/6-iodoacetamide (XRIA 5,6).

41. The composition of claim 34 wherein said analyte permeable matrix is selected from the group consisting of covalently crosslinked hydrogels, dialysis membranes, sol-gels, and combinations thereof.

42. The composition of claim 41 wherein said dialysis membranes have a molecular weight cut-off of about 1000 to about 25,000 Daltons.

43. The composition of claim 41 wherein said covalently crosslinked hydrogel is selected from the group consisting of polypeptides, polysaccharides, polysaccharide derivatives, polyvinyl alcohol, polyacrylic acid, polyacrylamide, polyethylene glycols, copolymers of styrene and maleic anhydride, copolymers of olefin and maleic anhydride, and copolymers of vinyl ether and maleic anhydride.

44. The composition of claim 43 wherein said said polyvinyl alcohol includes poly(vinyl alcohol), N-methyl-4(4'-formylstyryl)pyridinium acetal salts.

45. The composition of claim 41 wherein said sol-gel is selected from at least partially cured hydrolytically condensable siloxanes condensed with at least one water soluble organic polyol component.

46. The composition of claim 45 wherein said at least one water soluble organic polyol component is selected from glycerol, ethylene glycol, propylene glycol, and polyethylene glycol.

47. The composition of claim 45 further comprising at least one water soluble polymer component.

48. The composition of claim 47 wherein said at least one water soluble polymer component is selected from polyvinyl alcohol, copolymers of styrene and maleic anhydride, copolymers of olefin and maleic anhydride, and copolymers of vinyl ether and maleic anhydride, poly-(vinylsulfonic acid) salt, and polyvinyl pyrollidone.

49. The composition of claim 45 further comprising functionalized silicone additives.

50. The composition of claim 49 wherein said functionalized silicone additives contains organic functionality selected from the group consisting of alkyl, aryl, amine, amide, thiol, cyano, carboxyl, ester, olefinic, epoxy, silyl, nitro, and halogen.